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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/530,091	03/13/2006	Matthew S Gill	314-300810US	7528

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EXAMINER

MARTIN, PAUL C

ART UNIT	PAPER NUMBER
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1657

MAIL DATE	DELIVERY MODE
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07/26/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.		Applicant(s)	
	10/530,091		GILL ET AL.	
	Examiner		Art Unit	
	Paul C. Martin		1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 May 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-65 is/are pending in the application.
- 4a) Of the above claim(s) 23-65 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-22 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 31 March 2005 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>4/7/06</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1-65 are pending in this application.

Election/Restrictions

Applicant's election without traverse of Group I (Claims 1-22) in the reply filed on 05/22/07 is acknowledged. Claims 23-65 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse.

Claims 1-22 were examined on their merits.

Drawings

Color photographs and color drawings are not accepted unless a petition filed under 37 CFR 1.84(a)(2) is granted. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and, unless already present, an amendment to include the following language as the first paragraph of the brief description of the drawings section of the specification:

The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings and black and white photographs have been satisfied. See 37 CFR 1.84(b)(2).

The drawing (Fig. 4) is objected to under 37 CFR 1.83(a) because it fails to show the colors as described in the specification. Any structural detail that is essential for a proper understanding of the disclosed invention should be shown in the drawing. MPEP § 608.02(d). Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Specification

The use of the trademarks SYTOX TM, MILLI-Q TM and DYNABEADS TM has been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

Claim 1 is objected to because of the following informalities: The word "indicates", the phrase "is indicative" or the like should be inserted between "...test agents" and "that the..." in line 10 of the claim. Appropriate correction is required.

Claim 21 is objected to because of the following informalities: The word "from" appears to be misspelled in line 1 of the claim. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5, 6 and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite in that it fails to point out what is included or excluded by the claim language.

This claim is an omnibus type claim. Claims 5, 6 and 9 contain the trademark/trade names SYTOX™ or COPAS™ BIOSORT. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a fluorescent label and dispensing device respectively and, accordingly, the identification/description is indefinite.

Claims 4 and 6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 4 recites the broad recitation "substantially excluded from live eukaryotic cells", and the claim also recites "completely excluded from live eukaryotic cells" which is the narrower statement of the range/limitation. Claim 6 is rejected as being dependent upon rejected Claim 4.

Claims 16-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 16-18 are drawn to determining if test agents if test agents increase or decrease thermotolerance, oxidative stress or tolerance to a nematocide respectively. The claims are all dependent upon claim 1 however which is drawn to the determination of an increase or decrease in viability of nematodes exposed to one or more test agents. It is unclear if the steps of Claims 16-18 constitute an extra step in the method of Claim 1 or if the increases or decreases in tolerance in Claims 16-18 constitute a determination of viability as in Claim 1.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 19 and 20 rejected under 35 U.S.C. 102(b) as being anticipated by Comley *et al.* (1989).

Comley *et al.* teaches a method for quantifying microfilaria (nematodes) numbers and viability comprising: providing multiple 6-well microwell plates, each well containing one nematode, contacting the nematodes with anti-filarial drugs or solvent control, contacting the nematodes with the colorimetric label MTT (3-(4,5 dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide) and detecting the reduced MTT with a multi-well scanning spectrophotometer to ascertain the viability of the nematodes contacted with the drugs, wherein a decrease in viability is indicative of the nematodes being susceptible to the activity of the test agent (Pg. 78, Column 1, Lines 21-67 and Pg. 80, Table 1).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-3, 7, 8, 10-14, 19, 20 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Comley *et al.* (1989) in view of Verwaerde *et al.* (US 6,787,125 B1).

The teachings of Comley *et al.* were discussed above.

Comley *et al.* does not teach the use of a multiwell microtiter plates in 96, 100, 320, 384, 864 and 1536 well configurations, wherein the dispensing of the nematodes into the wells of the microtiter plates is performed using an automatic dispensing system, wherein the nematodes comprise genetic knockouts or wherein the nematodes are transgenics, wherein the nematodes comprise non-wildtype *C. elegans*, or wherein the detectable label is a fluorescent label and the detecting comprises detecting fluorescence in one or more wells comprising said microtiter plate with a fluorometer.

Verwaerde *et al.* teaches high-throughput screening methods using 6, 12, 24, 96, 384, 864 or 1536 well microtiter plates (Column 4, Lines 48-56), the use of transgenic or mutant *C. elegans* nematodes (Column 13, Lines 19-21), that other nematode species are useful in the method (Column 4, Lines 57-65), the use of a worm dispensing apparatus (Column 6, Lines 40-49), that the use of multiwell microplate readers can be used with a wide variety of detection methods, such as fluorescent, colorimetric, and spectrophotometric detection, and the detection of fluorescent detectable labels using a fluorometer (Column 6, Lines 60-67 and Column 7, Lines 1-3).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the colorimetric nematode viability screening method of Comley *et al.* with the high-throughput nematode screening method of Verwaerde *et al.* because the method of Verwaerde *et al.* presents improved aspects of screening over the method of Comley *et al.* alone.

One of ordinary skill in the art would have recognized that the multiwell plates in configurations other than the 6 well plates used by Comley *et al.* would have been functional variations thereof. One of ordinary skill in the art would have recognized that the fluorescent detectable labels and fluorometer detection devices were functional variations of the colorimetric label and spectrophotometer used by Comley *et al.* above. Further the use of a dispensing apparatus would have been recognized as an obvious automation of an activity previously performed by hand.

One of ordinary skill in the art would have recognized that the use of mutant (knock-outs, for example) or transgenic *C. elegans* would allow one to screen for or alternatively detect biochemical responses to environmental stimuli.

One of ordinary skill in the art would have been motivated to make this combination because the high-throughput methods of Verwaerde *et al.* represent improvements in efficiency and time in the screening method through the use of automation and replication of steps. There would have been a reasonable expectation of success in combining the two methods because both are drawn to similar methods of screening compounds using nematode worms.

Claims 1-3, 7-14, 19, 20 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Comley *et al.* (1989) in view of Verwaerde *et al.* as applied to Claims 1-3, 7, 8, 10-14, 19, 20 and 21 above, and further in view of Ferrante *et al.* (2002).

The teachings of Comley *et al.* and Verwaerde *et al.* were discussed above.

Neither Comley *et al.* nor Verwaerde *et al.* teaches the use of a COPAS™BIOSORT device.

Ferrante *et al.* teaches the use of the COPAS™BIOSORT device in fluorescence analysis of transgenic *C. elegans* and that the use of the device provides an improved signal to autofluorescence ratio and therefore, increased precision in detection (Lines 1-8 and 18-19).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the combined nematode screening methods of Comley *et al.* and Verwaerde *et al.* to include the use of the COPAS™BIOSORT device as taught by Ferrante *et al.* because one of ordinary skill would have recognized the device as a specific example of the worm dispensing apparatus as taught by Verwaerde *et al.* above. One of ordinary skill in the art would have been motivated to make this modification because of the advantage in increased precision in determining fluorescent signal from background autofluorescence. There would have been a reasonable expectation of success in making this modification because the use of fluorescence labeling is taught by Verwaerde *et al.* as a functionally equivalent technique of the colorimetric labeling method of Comley *et al.*, and further because Verwaerde *et al.* teaches the use of automated means of dispensing worms.

Claims 1-14, 19, 20 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Comley *et al.* (1989) in view of Verwaerde *et al.* as applied to Claims 1-3, 7, 8, 10-14, 19, 20 and 21 above, and further in view of Jain *et al.* (1993).

The teachings of Comley *et al.* and Verwaerde *et al.* were discussed above.

Neither Comley *et al.* nor Verwaerde *et al.* teach a method wherein the detectable fluorescent label is a label that penetrates compromised cell membranes, but is substantially or completely excluded from live eukaryotic cells or wherein the detectable label is SYTOX® blue, SYTOX® orange or propidium iodide.

Jain *et al.* teaches a method of detecting lethal injury or cell death in mutant *C. elegans* nematodes wherein morphological changes following ionomycin treatment in relation to increased Ca^{2+} and cell death is measured using the fluorescent probes Fluo-3/AM and propidium iodide and wherein the regions of cell death can be characterized by the fluorescent label (Pg. 575, Column 2, Lines 10-20 and Pg. 577, Fig. 5).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the teachings of Comley *et al.* and Verwaerde *et al.* for screening for the effects of compounds on nematodes with the use of the fluorescent detectable probe propidium iodide as taught by Jain *et al.* because this would allow one to accurately detect the loss of cellular viability in specific organs or tissue of the nematode worms in a high-throughput manner. One of ordinary skill in the art would have been motivated to make this modification because of the advantage of being able to detect what tissues or organs are specifically effected by a particular compound. There would have been a reasonable expectation of success in making this modification because all three methods are drawn to the characterization and detection of the effects of test compounds on nematode worms.

Claims 1-3, 7, 8, 10-17, 19, 20 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Comley *et al.* (1989) in view of Verwaerde *et al.* (US 6,787,125 B1) and Lithgow *et al.* (1995).

The teachings of Comley *et al.* and Verwaerde *et al.* were discussed above.

Neither Comley *et al.* nor Verwaerde *et al.* teach the use of thermotolerant nematodes, subjecting the nematodes to heat and determining if test agents increase or decrease thermotolerance in nematodes, subjecting nematodes to an agent that increases oxidative stress and determining if test agents increase or decrease tolerance of oxidative stress in nematodes.

Lithgow *et al.* teaches the use of thermotolerant mutant *C.elegans* in assays wherein viability between the mutant nematodes and wild type nematodes are compared after exposure to thermal stress (Pg. 7541, Fig. 1), that the mutant nematodes also have greater resistance to oxidative stress caused by agents such as hydrogen peroxide and paraquat (Pg. 7540, Column 2, Lines 3-6) and that there is a relationship between thermotolerance and longevity and that since stress-response genes are conserved in diverse species that the relationship may also be found in mammals (Pg. 7544, Column 1, Lines 53-61).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the combined teachings of Comley *et al.* and Verwaerde *et al.* for assaying nematode viability to include the use of thermotolerant nematodes and the further steps of exposing the nematodes to heat or oxidative agents and determining an increase or decrease in tolerance thereof in the presence of test agents because the use of thermotolerant nematodes would have been a matter of experimental design on the part of the ordinary artisan.

Further, the use of heat and oxidative agents on thermotolerant mutants was known at the time of the inventions as taught by Lithgow *et al.* above. One of ordinary skill in the art would have been motivated to make these modifications because the identification of test agents which can increase or decrease tolerance to oxidative stress and/or the thermotolerance of long lived mutant nematodes would provide insight into the aging process of other species such as mammals. There would have been a reasonable expectation of success in making these modifications, because all three methods are drawn to the use of nematodes in viability assays.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

No Claims are allowed.

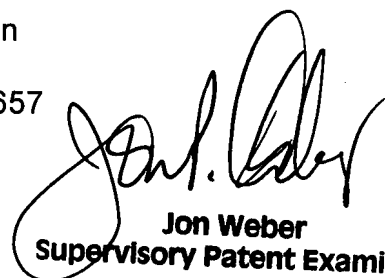
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul C. Martin whose telephone number is 571-272-3348. The examiner can normally be reached on M-F 8am-4:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Paul Martin
Examiner
Art Unit 1657

7/10/07



Jon Weber
Supervisory Patent Examiner